



Amendments to the Specification

Please replace the paragraph on page 23, at lines 5-6, with the following amended paragraph:

lco375-pbgds (32 mer) coding region 5' end w/ EcoRI site sense
5' CGT GGA ATT CAT GAG AGT GAT TCG CGT GGG TA 3' (SEQ. ID. NO.: 25)

Please replace the paragraph on page 23, at lines 8-9, with the following amended paragraph:

lco376-pbgda (47 mer) coding region 3' end w/ HindIII site antisense
5' GGA GAA GCT TAT TAA TGG GCA TCG TTC AAT TGC CGT GCA ACA TCC AG 3' (SEQ. ID. NO.: 24)

Please replace the paragraph on page 23, at lines 11-12, with the following amended paragraph:

lco379-esnonc (20 mer) erythropoietic form non-coding sense
5' TCG CCT CCC TCT AGT CTC TG 3' (SEQ. ID. NO.: 25)

Please replace the paragraph on page 23, at lines 14-15, with the following amended paragraph:

lco380-sinter (21 mer) internal coding sense
5' CAG CAG GAG TTC AGT GCC ATC 3' (SEQ. ID. NO.: 26)

Please replace the paragraph on page 23, at lines 17-18, with the following amended paragraph:

lco381-ainter (21 mer) internal coding antisense
5' GAT GGC ACT GAA CTC CTG CTG 3' (SEQ. ID. NO.: 27)

Please replace the paragraph on page 24, at lines 1-2, with the following amended paragraph:

lco382-anonc (20 mer) non-coding antisense
5' CAG CAA CCC AGG CAT CTG TG 3' (SEQ. ID. NO.: 28)

Please replace the paragraph on page 24, at lines 4-5, with the following amended paragraph:

Ico383-pSKT7 (22 mer) pBluescript T7 promoter
5' GTA ATA CGA CTC ACT ATA GGG C 3' (SEQ. ID. NO.: 29)

Please replace the paragraph on page 24, at lines 7-8, with the following amended paragraph:

Ico384- pSKpjrev (22 mer) pBluescript reverse1
5' CTA AAG GGA ACA AAA GCT GGA G 3' (SEQ. ID. NO.: 30)

Please replace the paragraph on page 24, at lines 10-11, with the following amended paragraph:

Ico385- pSKrev (21 mer) pBluescript reverse2
5' CAG CTA TGA CCA TGA TTA CGC 3' (SEQ. ID. NO.: 31)

Please insert the following new paragraph at page 27, line 25:

(DNA sequence is SEQ ID NO:32; amino acid sequence is SEQ ID NO:33).

Please replace the paragraph on page 31, at lines 14-16, with the following amended paragraph:

ICO386 (54 mer) Construction of plasmid pExp1
5' AAT TCT AAC ATA AGT TAA GGA GGA AAA AAA AAT GAG AGT TAT TCG TGT CGG
TAC 3' (SEQ. ID. NO.: 45)

Please replace the paragraph on page 31, at lines 18-19, with the following amended paragraph:

ICO387 (46 mer) Construction of plasmid pExp1
5' CGA CAC GAA TAA CTC TCA TTT TTT TTT CCT CCT TAA CTT ATG TTA G 3' (SEQ. ID. NO.: 46)

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Please replace the paragraph on page 31, at lines 21-22, with the following amended paragraph:

ICO424 (32 mer) Construction of plasmid pExp1-M2
5' GAT CAC TCA TGT TTG ACA GCT TAT CAT CGA TT 3' (SEQ. ID. NO.: 47)

Please replace the paragraph on page 31, at lines 24-25, with the following amended paragraph:

ICO425 (31 mer) Construction of plasmid pExp1-M2
5' AGC TAA TCG ATG ATA AGC GTC AAA CAT GAG T 3' (SEQ. ID. NO.: 48)

Please replace the paragraph on page 31, at lines 27-28, with the following amended paragraph:

ICO437 (32 mer) Amplification of product P1
5' AGT CAG AAT TCA GAC GCA CGG CGG TAC GAT AA 3' (SEQ. ID. NO.: 49)

Please replace the paragraph on page 31, at lines 30-31, with the following amended paragraph:

ICO438 (32 mer) Amplification of product P1
5' ATT CAC TCG AGG TCA CCA TCG GTA CCA GTT CA 3' (SEQ. ID. NO.: 50)

Please replace the paragraph on page 31, at lines 33-34, with the following amended paragraph:

ICO440 (32 mer) Amplification of product P2
5' AGA TCA AGC TTC GGC CAG ACG CAG GTT ATC TA 3' (SEQ. ID. NO.: 51)

Please replace the paragraph on page 32, at lines 1-2, with the following amended paragraph:

ICO505 (34 mer) Amplification of product P2
5' ATA CAC TCG AGA CCG GCA TGA GTA TCC TTG TCA C 3' (SEQ. ID. NO.: 52)

Please replace the paragraph on page 32, at lines 4-5, with the following amended paragraph:

ICO510 (30 mer) Amplification of Cam gene
5' ACT GAC CTC GAG CGG CAC GTA AGA GGT TCC 3' (SEQ. ID. NO.: 53)

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*Please replace the paragraph on page 32, at lines 7-8,
with the following amended paragraph:*

ICO511 (29 mer) Amplification of Cam gene
5' ACT GAA CTC GAG AAT TAC GCC CCG CCC TG 3' (SEQ. ID. NO.: 54)

*Please replace the paragraph on page 43, at lines 4-7,
with the following amended paragraph:*

Non-erythropoietic PBGD form (nPBGD):
Met-Ser-Gly-Asn-Gly-Asn-Ala-Ala-Ala-Thr-Ala-Glu-Glu-Asn-Ser-Pro-Lys-Met-Arg-Val...(SEQ. ID. NO.: 55).
ATG-TCT-GGT-AAC-GGC-ATT-GCG-GCT-GCA-ACG-GCG-GAA-GAA-AAC-AGC-CCA-
AAG-ATG-AGA-GTG..(SEQ. ID. NO.: 56)

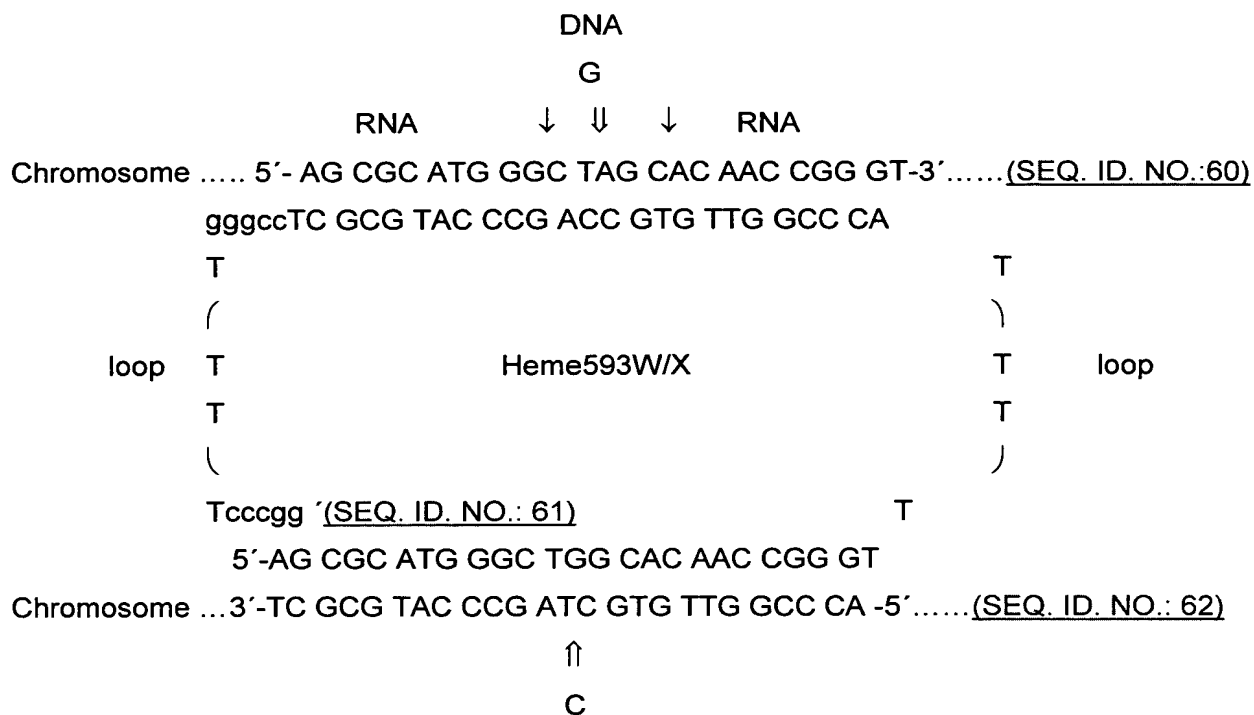
*Please replace the paragraph on page 48, at lines 22-
24, with the following amended paragraph:*

Normal Chromosomal Sequence:
5'-AG CGC ATG GGC TGG CAC AAC CGG GT-3' (SEQ. ID. NO.: 57)
Gln Arg Met Gly Trp His Asn Arg Val (SEQ. ID. NO.: 58)

*Please replace the paragraph on page 48, at lines 26-
27, with the following amended paragraph:*

AIP Chromosomal Sequence:
5'- AG CGC ATG GGC TAG CAC AAC CGG GT-3' (SEQ. ID. NO.: 59)
Stop

Please replace the paragraph on page 49, at lines 3-17, with the following amended paragraph:



Please replace the paragraph on page 81, at lines 18 to page 82, line 2, with the following amended paragraph:

A liver from a healthy mouse was homogenized and the total RNA was extracted. Complementary DNA was synthesized from total RNA using reverse transcriptase from murine leukemia virus and random priming (First-Strand cDNA Synthesis Kit, Amersham Pharmacia Biotech). The PBGD cDNA housekeeping form was amplified by using nested primers in the polymerase chain reaction (PCR). In the first primer pair the forward primer was 5'-GGAGTCATGTCCGGTAACG-3' (SEQ. ID. NO.:41) and the backward 5'-CAGACCAGTTAGCGCACATC-3' (SEQ. ID. NO.:42). In the second primer pair the forward primer was 5'-CGCGGGGTGACGCCACCATGTCCGGTAACGGCGGC-3' (SEQ. ID. NO.:43) that contained the restriction site *Sall* and a Kozak site necessary for optimal translation and the backward primer was 5'-CCCGGGGGTACCTTAGCGCACATCATTAAAG-3' (SEQ. ID. NO.:44) that contained a *KpnI* restriction site. The amplified PBGD was digested by *Sall* and *KpnI* and ligated into the plasmid pNGVL3-GTC1 that was digested with the same restriction enzymes.

The vector pNGVL3-GTC1 contains a cytomegalovirus (CMV) promoter and a kanamycin resistance gene obtained from National Gene Vector Laboratory (University of Michigan). *Escherichia coli* was transformed by the recombinant vector and the transformed bacteria was selected by the antibiotic kanamycin. The recombinant plasmid, pNGVL3-GTC1-PBGD, was isolated from selected clones and the PBGD cDNA insert was confirmed by restriction enzyme analysis and sequencing.

Please replace the paragraph on page 125, at line 26 to page 126, line 5, with the following amended paragraph:

As the same ALAD polypeptide is expressed in all cell types (1) any tissue can serve as a source for cloning. Spleen cDNA (made by Donald Rao using BRL Superscript II with 500 ng Clontech poly-A RNA from a pool of different donors, catalogue # 6542-1, in 20 μ l reaction volumes per manufacturer's instructions) was used. One μ l of cDNA (approximately 25 μ g) was amplified with Advantage cDNA polymerase mix (Clontech Catalogue # 8417-1) with 0.2mM dNTP and 0.4 μ M each of ICO549 (5' ATCCATGAATTCCACGCAATGC AGCCCCAGTC 3') (SEQ. ID. NO.: 34) and ICO550 (5' AGTCGTAAGCTTGCCTGGCA CTGTCCTCCATC 3') (SEQ. ID. NO.: 35) in 50 μ l reaction volumes. Two cycle PCR was used with an initial heat denaturation step at 94°C for 100 seconds followed by 28 cycles of 96°C for 20 seconds and 72°C for 2 minutes. A final extension of 7 minutes at 72°C was used at the end to ensure that the extension products were filled out. One μ l of this PCR mix was again amplified exactly as described above and cloned into pBluescript II SK- (Stratagene, catalogue # 212206), linearized with *EcoR* I and *Hind* III after purification (using GEANECLEAN III, from BIO 101 catalogue # 1001-600) and digestion with the same two enzymes (see Figure 37, A and B).

Please replace the paragraph on page 126, at line 9-15, with the following amended paragraph:

Four plasmid clones from the above ligation viz. pBlueAlaD-1-4 were sequenced with the Big Dye terminator cycle sequencing kit from PE/ABI catalogue # 4303152. Three vector primers, ICO383 (5' GTAATACGACTCACTATA GGGC 3' (SEQ. ID. NO.: 36)), ICO384 (5' CTAAAGGGAACAAAAGCTGGAG 3' (SEQ. ID. NO.: 37)) and IC0618 (5- GCGCGTAATACGACTCACTA 3 (SEQ. ID. NO.: 38)) and two ALAD-specific primers, ICO616

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(5' CCTACGCTGTGTCTTGATCT 3' (SEQ. ID. NO.: 39)) and ICO617 (5' GGCTT CACCATGAGCATGTC 3' (SEQ. ID. NO.: 34)) were used. The results are tabulated in Table 46.